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Received 21 June 1988.
Accepted 16 November 1988.

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0041-1337/89/4706-0971$02.00/0
TRANSPLANTATION

Vol. 47, 971-977, No. 6, June 1989
Printed in U.S.A.

HEPATIC ARTERY THROMBOSIS AFTER PEDIATRIC LIVER TRANSPLANTATION—A MEDICAL OR SURGICAL EVENT?[1]

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Hepatic artery thrombosis (HAT) is one of the most serious complications after orthotopic liver transplantation, and is associated with a high morbidity and mortality. This study retrospectively reviewed 66 liver transplants in children under the age of 10 years during a year-long period at a single institution. A total of 28 perioperative variables were analyzed to identify responsible factors of HAT. Of the 66 children, 18 (26%) developed HAT within 15 days after the transplant (HAT group); 29 (42%) had an uneventful postoperative course (control group). To avoid the possible influence of other complications 19 patients were excluded. Of the variables compared between the 2 study groups, three surgical factors (diameter of the hepatic artery—greater or less than 3 mm; type of arterial anastomosis—end-to-end versus the use of an iliac graft or aortic conduit; and number of times the anastomosis was redone—one versus more than one), were found to be significantly different ($P<.05$) between HAT and control groups. Two medical factors also were significantly different: the use of intraoperative transfusion of fresh frozen plasma (FFP) and the administration of postoperative prophylactic anticoagulant treatment. A heparin and dextran-40 protocol appeared to be effective in preventing HAT ($P<.02$). Moreover, after multivariate analysis, anticoagulation therapy was demonstrated to

[1]This work was supported by Research Grants from the Veterans Administration (Project Grant DK 29961), from the NIDDK (AM 32556), and from the NIAAA (AA06601).

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be the major independent variable influencing HAT. A better definition of factors responsible for the occurrence of HAT is required. This study should help in formulating effective methods to decrease the incidence of this dreaded complication after liver transplantation.

Thrombosis of the hepatic artery (HAT)* is common, and is one of the most serious complications following orthotopic liver transplantation (OLTx). Several reports on this subject (*1–3*) have failed to identify possible risk factors that may be related to thrombosis of the hepatic artery. Nonetheless a clear definition of the responsible factors is necessary in order to reduce its incidence and to formulate guidelines and protocols for the management of this dreaded complication.

In the present study two homogeneous and comparable populations—pediatric liver recipients who developed thrombosis of the hepatic artery after OLTx and those who did not—have been identified. An accurate statistical comparison between these two groups has been carried out in an attempt to identify the responsible factors leading to thrombosis.

MATERIALS AND METHODS

Patient population (Table 1). During the calendar year 1986, 66 consecutive children under the age of 10 years received primary liver transplant at the Children's Hospital of Pittsburgh.

The methods of patient selection, techniques for orthotopic liver transplantation, protocols for immunosuppressive management and postoperative care have been described in detail previously (*4–6*).

A total of 18 children with hepatic artery thrombosis that occurred within 15 days of transplantation were included in the HAT group (26% of the whole series). The diagnosis of HAT was usually suspected in the presence of fulminant hepatic necrosis, biliary leak, or recurrent bacteremia, and was always confirmed by sonography and/or angiography.

A group of 19 children with a major posttransplant complication (i.e., primary nonfunction of the graft, sepsis, reoperation for bleeding, bowel perforation, and biliary leak) were excluded from the study, and only 29 patients (42%) with a relatively uneventful postoperative course during the first month were taken as a control group. At least one sonogram was performed routinely in all the patients in this study—controls, HAT, and excluded ones—to confirm hepatic artery patency. If a pulsatile artery was not clearly seen, an angiographic study was performed in each patient regardless of group status. Posttransplant management of all recipients was also comparable in all the patients.

The arterial reconstructions were performed with an end-to-end anastomosis (EEA) between donor and recipient arteries in 40 instances (13 of 18 patients in the HAT group and 17 out of 29 controls). In seven patients either a donor iliac artery allograft or an aortic conduit was eventually placed on the infrarenal aorta and then brought up to the liver hilum through a retropancreatic tunnel (*7*) (Table 2). The anastomoses were performed mainly at the level of the celiac axis or common hepatic artery of the recipient (61.1% and 62.1% of cases in the two groups, respectively). A complete list of the levels of anastomosis is summarized in Table 2. In two control patients the splenic artery was ligated close to the celiac axis after an EEA of the hepatic artery in an attempt to prevent a possible "steal" from the small-diameter hepatic artery anastomosis.

A running continuous suture with a "growth factor" was used for most of the arterial anastomoses (*8*); interrupted suture was used for the anterior wall of the anastomosis in 5 of 29 controls and in 2 of 18 patients who suffered thrombosis of the hepatic artery, and 7–0 monofilament (Prolene-Ethicon or Novafil-Davis-Geck) was used to perform all the anastomoses.

A total of 28 perioperative variables from both the donor and recipient for each transplant were recorded and are listed in Tables 1, 2, and 3. In particular, information about the preoperative coagulation status of all patients was collected for the analysis. Intraoperatively, the worst coagulation status (i.e., the lowest PT and PTT, and the highest hematocrit and platelet count) was also evaluated. Blood loss and the quantity and type of transfusions have been analyzed as well (*9–11*). The blood volumes required to replace the blood loss were estimated as 70 ml/kg in children older than 2 years and 80 ml/kg in patients 0–2 years of age.

The anticoagulation therapy was administered in a random fashion because of the preliminary nature of this therapeutic investigation. Dosages of the medications used were as follows:

Dextran-40: 5–10 ml/hr starting intraoperatively immediately after the transplant and continued for 5 days.

Heparin: 50 U/kg divided into 2 daily doses subcutaneously, starting postoperatively as soon as the PT and PTT were less than 20 and 40 sec, respectively. Heparin was discontinued at the time of discharge.

Aspirin (ASA): 20 mg orally or as a suppository for children weighing <10 kg; 40 mg for children >10 kg. Therapy was continued for at least 3 months.

Persantine (dypiridamole): 12.5 mg p.o. 3 times a day for children weighing <20 kg; 25 mg p.o. 3 times a day for children >20 kg starting from the 5th or 6th postoperative day and continued for at least 3 months.

Statistical analysis. The variables listed in Tables 1, 2, and 3 were investigated to determine any statistically significant difference ($P<.05$) between "cases" (HAT-group) and "controls" (uneventful postoperative course).

When this many comparisons are undertaken, the multiple comparison problem comes into play; in fact with 28 variables examined, there is about 76% probability of finding at least one variable that will be statistically significant and associated with group status (cases or controls) by chance alone; thus statistical tests of significance were employed in an exploratory manner.

To identify continuous variables both parametric and nonparametric tests were used. The Student's *t* test and chi-square were employed; in addition the nonparametric Wilcoxon and median tests were used for differences in central tendency.

The logistic regression model finally provided an estimation of the risk of having a hepatic artery thrombosis (odds ratio) in groups defined by the kind of prophylactic anticoagulative treatment used postoperatively.

The entire statistical analysis was performed on an IBM-PC computer utilizing the BMDP statistical software package (*12, 13*).

RESULTS

During the year 1986, 66 children under 10 years of age received primary liver transplants at the Children's Hospital of Pittsburgh. Thrombosis of the hepatic artery occurred within 15 days after the transplant (5.3±1.2 days) in 18 patients (26% of the cases) and they formed the HAT group. Of the remaining 48 patients, 19 developed other major complications and thus were excluded. The control group consisted of 29 children (42% of the cases) with a relatively uneventful postoperative course.

Demographics for the 47 patients studied are presented in Table 1. No statistical difference was found in terms of age, sex, body weight, blood type predominance, and indication for OLTx (biliary atresia in more than 75% of the cases) between the HAT group and controls.

The surgically related factors that were analyzed are listed in Table 2. Of 18 patients who developed thrombosis, 10 had a hepatic artery diameter of ≤3 mm, whereas only 7 of 29 controls

* Abbreviations: EEA, end-to-end anastomosis; HAT, hepatic artery thrombosis; FFP, fresh frozen plasma; OLTx, orthotopic liver transplantation.

TABLE 1. General characteristics of pediatric liver transplant patients (under 10 years of age) listed by group status

(No.)	Variable	Hepatic Artery Thrombosis	Controls	P value
Cases:		18	29	
(1)	Age (years):			
	Mean ± SE	2.9±0.65	2.6±0.3	
	Median	2.0	2.3	NS
	Minimum-maximum	0.1–9.7	0.5–7.7	
(2)	Sex (male/female):	7/11 (38.9%)/(61.1%)	13/16 (44.8%)/(55.2%)	NS
(3)	Body weight (kg) (mean ± SE):	11.4±1.46	12.7±1.04	NS
(4)	Blood type			
	0	11 (61.1%)	12 (41.4%)	NS
	A	5 (27.8%)	10 (34.5%)	
	B	2 (11.1%)	6 (20.7%)	
	AB	0 (0%)	1 (3.4%)	
(5)	Diagnosis:			
	Biliary atresia	14 (77.8%)	23 (79.7%)	NS
	Other (metabolic errors, congenital hepatic fibrosis, hepatitis, etc.)	4 (22.2%)	6 (17.2%)	

TABLE 2. Surgical factors analyzed for possible relationship with the occurrence of thrombosis of the hepatic artery

(No.)	Variable	Hepatic artery thrombosis	Controls	P value
(6)	Size of the hepatic artery (diameter):			<.05
	≤3 mm.	10 (55.6%)	7 (24.1%)	
	>3 mm.	8 (44.4%)	22 (75.9%)	
(7)	Level of the anastomosis:			NS
	Celiac axis	6 (33.3%)	10 (34.5%)	
	Common hepatic artery	5 (27.8%)	8 (27.6%)	
	Gastroduodenal takeoff	1 (5.6%)	6 (20.7%)	
	Splenic artery	1 (5.6%)	2 (6.9%)	
	Aorta	5 (27.8%)	3 (10.3%)	
(8)	Anomalies in arterial anatomy of the donor liver that required a backtable reconstruction:			NS
	No	14 (77.8%)	28 (96.6%)	
	Yes	4 (22.2%)	1 (3.4%)	
(9)	Kind of arterial reconstruction:			<.05
	End-to-end	13 (72.2%)	27 (93.1%)	
	Other (iliac graft, aortic conduit, etc.)	5 (27.8%)	2 (6.8%)	
(10)	No. of times the anastomosis was done intraoperatively:			<.02
	One	12 (66.7%)	28 (96.6%)	
	Two or more	6 (33.3%)	1 (3.4%)	
(11)	Suture material:			NS
	Prolene (Ethicon)	16 (88.9%)	21 (72.4%)	
	Novafil (Davis-Geck)	2 (11.1%)	8 (27.6%)	

had a hepatic artery of this size ($P<.05$). The diameter of the artery was determined intraoperatively just prior to the actual anastomosis using the caliber on the knife stick. The number of times the anastomosis was redone to achieve a satisfactory intraoperative result was significantly associated with HAT. In fact, two or more attempts at arterial anastomoses occurred in 6 of 18 patients in the HAT group (33%) but in only 1 of 29 controls (3.4%) ($P<0.02$). The use of an arterial graft was associated with an increased risk of thrombosis, and 5 of 7 (70%) children with arterial reconstructions that required the use of iliac artery grafts (3 cases) or aortic conduit (2 cases) developed HAT. On the other hand, a significative difference ($P<.05$) was found between the number of patients who underwent an EEA in each group (13/18 patients of the HAT group (72.2%) versus 27/29 patients of the control group (93%). None of the children with aortic conduits had a previously attempted hepatic artery EEA. Of 7 arterial grafts, 5 were preceded by an initial attempt at a direct anastomosis.

The level of anastomosis (celiac axis or common hepatic artery accounting for over 61% of cases in both groups) did not show any difference between HAT and controls. Neither the suture material (Prolene versus Novafil) nor the technique of continuous versus interrupted sutures had any significant impact on the incidence of HAT.

Medical-related factors collected for this analysis are presented in Table 3 (parts I and II). All donor livers but two were procured by the rapid-flush technique (*14, 15*) and were preserved in Euro-Collins solution. All grafts experienced a comparable total ischemia time (6.8 ± 2.3 hr). The number of non-ABO compatible livers used in each group was not statistically different.

The preoperative coagulation status and intraoperative co-

TABLE 3. Medical factors

I. Medical factors possibly associated with thrombosis of the hepatic artery

(No.)	Variable	Hepatic artery thrombosis	Control	P value
(12)	ABO compatibility of donor and recipient;			NS
	Compatible	16 (88.9%)	27 (93.1%)	
	Not compatible	2 (11.1%)	2 (6.9%)	
	Preoperative coagulation profile (mean ± SE):			NS
(13)	PT (sec)	15.2±0.9	15.3±0.5	
(14)	PTT (sec)	34.5±2.8	35.8±2.3	
(15)	HTc (%)	34.2±1.1	37.6±7.5	
(16)	Plat. ($\times 10^3$)	244±34	182±19	
	Intraoperative coagulation profile (mean ± SE):			NS
(17)	PT (sec)	14.3±0.2	14.8±0.4	
(18)	PTT (sec)	33.0±0.7	34.1±1.5	
(19)	HTc (%)	42.3±1.6	41.9±0.5	
(20)	Plat. ($\times 10^3$)	219±23	199±16	
(21)	Blood loss (ml)			NS
	Range	960–8600	260–13550	
	Mean ± SE	2781±355	3018±615	

II. Medical factors (intraoperative transfusion and anticoagulant prophylactic treatments)

No.	Transfusions and anticoagulants	YES		P value	NO	
		Thrombosed	Control		Thrombosed	Controls
	Type of transfusions:					
(22)	Whole blood	4 (23.5%)	4 (13.5%)	NS	13 (76.5%)	25 (86.2%)
(23)	FFP	16 (94.1%)	20 (69.0%)	<.05	1 (5.9%)	9 (31.0%)
(24)	Platelets	11 (64.7%)	12 (41.4)	NS	6 (35.3%)	17 (58.6%)
	Perioperative anticoagulant therapy	9 (50%)	3 (10.9%)	<.01	9 (50%)	26 (89.7%)
	Influence of different anticoagulation regimens:					
(25)	Aspirin	6 (33.3%)	17 (58.6%)	NS	12 (66.7%)	12 (41.4%)
(26)	Persantin	4 (22.2%)	9 (31.0%)	NS	14 (77.8%)	20 (69%)
(27)	Dextran-40	5 (27.8%)	20 (69.0%)	<.02	13 (72.2%)	9 (31.0%)
(28)	Heparin	2 (11.1%)	15 (51.7%)	<.02	16 (88.9%)	14 (48.3%)

agulation parameters were similar in both the HAT group and controls. The mean blood loss (2781±355 ml in the HAT versus 3018±615 ml in the controls), and transfusion requirements (4.1±1.3 blood volumes in the HAT group versus 3.9±0.8 blood volumes in the control patients) were not significantly different. The influence of the different components of the transfusions (whole blood, fresh frozen plasma, platelets) was compared between the two groups. This evaluation considered only whether patients did or did not receive one of these blood components. The incidence of HAT was significantly higher ($P<.05$) in children who received an intraoperative transfusion of fresh frozen plasma compared with children who did not receive FFP at all (Table 3, part II). No differences were found with respect to transfusion of whole blood or platelets. Epsilon-Aminocaproic acid (Amicar) was never used intraoperatively and postoperatively in the present series.

The use of postoperative anticoagulation correlated significantly ($P<.01$) with the occurrence of HAT; it was administered in almost 90% of the controls, while only 50% of the patients who eventually developed thrombosis received it. Ten different combinations of dextran-40, heparin, aspirin, and persantine were used in a random fashion considering the introductory purpose of this study in investigating the effect of postoperative anticoagulation. Dextran-40 followed by heparin was the most frequent protocol and was used in 12 cases (10 controls and 2 HAT). The aspirin-dextran-persantine combination was employed in 7 cases, and the dextran-heparin-aspirin in 5; The remaining combinations were varied.

The use of dextran-40 and heparin significantly correlated with nonthrombosis status ($P<.02$); furthermore the P value for aspirin (<.058) approached statistical significance (Table 3, part II). Hemorrhage during the anticoagulant treatment occurred in three cases in the control group and in 2 cases in the HAT group (no statistical differences); in 4 out of 5 cases a temporary 50% reduction in the dose of heparin was able to control the problem without further intervention. Only one control patient (2% of the total series) required an exploratory laparotomy along with discontinuation of the anticoagulation treatment.

The risk (odds ratio) of developing HAT according to whether or not each medication was employed as a prophylactic treatment is presented in Figure 1. The risk of thrombosis was almost 8.6 times greater in patients who did not receive any anticoagulation therapy than in patients who received heparin. This odds ratio was 5.8 for dextran, 1.8 for aspirin, and 1.6 for persantine.

A more detailed (univariate and multivariate) analysis of the five variables that were found to have a significant influence

on the occurrence of HAT revealed that the anticoagulation treatment was the only independent variable, with a coefficient of 11.7 belonging to heparin (Table 4). Further adjustments in the statistical analysis for heparin treatment demonstrated that the number of times the anastomosis was redone intraoperatively was the second independent variable influencing thrombosis. Dextran treatment did not appear in this second step of the multivariate analysis because it was employed with heparin most of the time. The same reasoning should be considered for the other two surgical variables (i.e., diameter of the artery and type of reconstruction), which did not exhibit significance independently after a further adjustment for the variable corresponding to the number of times the anastomosis was redone. In fact, all three surgical factors are strictly interrelated—and, most of the time, they occurred together during the operation. Finally, with further adjustments in the statistical review, aspirin with a coefficient of 5.3 was demonstrated to be the third most important factor related to the occurrence of thrombosis. The use of fresh frozen plasma did not demonstrate significance during this multivariate statistical study. A histogram summarizing the influence of these two medical and three surgical factors is shown in Figure 2.

DISCUSSION

Hepatic artery thrombosis after liver transplantation is a devastating event associated with a very high rate of graft-related sepsis and significant mortality (*1*). Its overall incidence is about 7–8%; however HAT has been reported to occur in about 4% of adult patients (*1, 3*), 12% of pediatric cases (under 18 years old) (*1*), and as many as 30% of children under the age of one year (*16*).

Hepatic artery thrombosis usually occurs early in the postoperative period. The clinical picture is varied and consists of a spectrum of fulminant hepatic necrosis, delayed biliary leak, or recurrent bacteremia (*1*). Late thrombosis may also occur several months after transplantation and is usually associated with single or multiple bile duct strictures or with relapsing bacteremia. Changes in liver function studies are minimal in cases of late thrombosis because of partial compensation of the hepatic arterial blood supply via collaterals around the liver (*2*). In the present series, late thrombosis occurred in 4 patients, after a mean interval of 195 days (range 96–240) after the transplant. These patients with late thrombosis have been excluded from the HAT group of this study.

In this study three "surgical" factors—the diameter of the hepatic artery (≤3 mm), the type of arterial anastomosis (end-to-end hepatic arterial versus other reconstructions such as use of iliac arterial grafts or aortic conduits), and multiple revisions of the arterial anastomosis to achieve a satisfactory intraoperative result—were found to be significantly different ($P<.05$) when comparing the HAT and the control groups. Similarly, two "medical" factors, consisting of intraoperative administra-

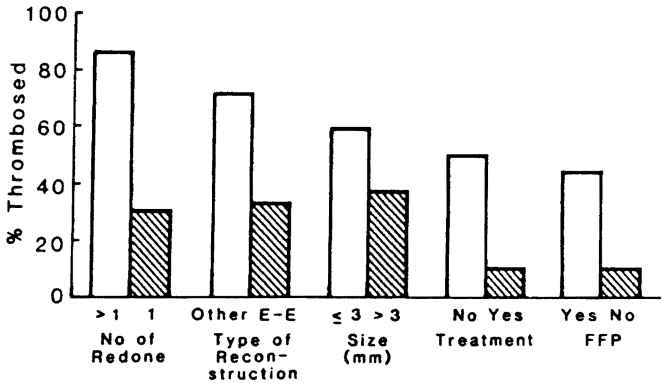

FIGURE 1. Relative risk (odds ratio) of thrombosis according to different anticoagulative regimens. For instance, the risk of developing thrombosis in a patient not treated with dextran is 5.8 times higher than a patient not given dextran in the prophylactic anticoagulative treatment.

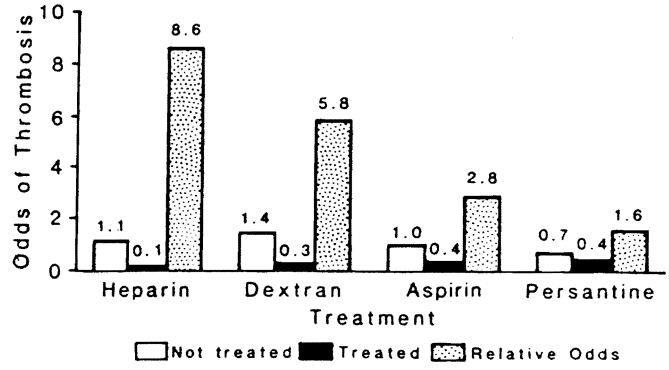

FIGURE 2. Relative influence of medical and surgical factors on the incidence of hepatic artery thrombosis after liver transplantation in children. Negative surgical factors exert a stronger effect on the incidence of thrombosis than medical factors (first three empty columns). Nevertheless, favorable medical factors clearly decrease the incidence of thrombosis (last two dotted columns). (No. of redone) number of times the anastomosis was redone (>1: more than one); (other) use of iliac graft, aortic conduit etc., (E-E) end-to-end anastomosis; (Size [mm]) diameter of the artery (greater or less than 3 mm); (Treatment) use of prophylactic anticoagulative treatment (Yes: used, No: not used). (FFP) fresh frozen plasma.

TABLE 4. Variate analysis of the surgical and medical risk factors of hepatic artery thrombosis after OLTx in children

Variables		Univariate odds ratio (95% confidence interval)	Multivariate odds ratio (95% confidence interval)
Size of hepatic artery (<3 mm vs. >3 mm)		3.93 (1.11, 13.8)	—
How many reconstructions of the hepatic artery (one vs. more than one)		14.0 (1.52, 129.2)	11.02 (1.0, 121.6)
Type of reconstruction (end-to-end vs. other reconstruction)		5.19 (0.89, 30.4)	—
FFP (fresh frozen plasma): intraoperative transfusion (some vs. none)		7.20 (0.82, 62.9)	—
Dextran-40	(Yes vs. no)	5.78 (1.58, 21.14)	—
Persantin	(Yes vs. no)	1.57 (0.40, 6.45)	—
Heparin	(Yes vs. no)	8.57 (1.66, 44.2)	11.7 (1.6, 82.5)
Aspirin	(Yes vs. no)	2.83 (0.83, 9.67)	5.3 (1.06, 26.8)

tion of FFP, and postoperative anticoagulant treatment with either heparin or dextran-40, were also found to be statistically different.

The resistance to the blood flow of any vessel is inversely proportional to its crossectional area; therefore the diameter of the hepatic artery is an obvious factor influencing the patency rate of the anastomosis. In fact, more than half the cases involving a hepatic artery with a diameter of less than 3 mm developed thrombosis, while 76% of the arteries with a diameter greater than 3 mm did not thrombose. Body weight and age of the child were not significantly different when HAT patients and controls were compared—however, there was an apparent trend correlating these variables with the size of the recipient hepatic artery, although this was not statistically significant. Moreover, in pediatric liver transplantation it is not uncommon to observe a lack of correlation between the size of the patient and the diameter of the hepatic artery. This is due to the hemodynamic derangement related to the liver disease, which is the most important factor in determining the arterial supply to the organ.

A higher incidence of HAT has been reported in association with the use of iliac arterial grafts and aortic conduits (*1, 17*). In the present series, the use of vascular allografts has been confirmed to be a risk factor in the development of early thrombosis, at least in children. Of 7 (70%) of the arterial reconstructions that required an iliac allograft or aortic conduit, 5 (70%) eventually thrombosed. Vascular grafts create turbulence, and this may be a factor in causing thrombosis. All grafts, in fact, were placed in the infrarenal position, with a possible turbulent inflow due to the position and length of the conduit. The supraceliac aorta may be a more favorable inflow location, although this technique deserves thorough examination. Rejection mechanisms directed at the vascular endothelial cell may offer another possible explanation (*18*).

The third significant surgical risk factor for thrombosis was the number of times the anastomosis had to be redone. Obviously the more times the anastomosis is redone, the greater the risk of intimal dissection, kinking, and excessive shortening of the vessel. Assessment of the adequacy of anastomosis by palpation of a thrill is quite subjective. Use of electromagnetic flow probes to accurately determine blood flow and assess the risk of HAT has recently been reported (*19*). Although determination of flow using this modality in small vessels is also subject to speculation, our preliminary data in pediatric recipients suggest that a flow rate <60 ml/min significantly increases the incidence of HAT (Yanaga, et al., manuscript submitted).

The three surgical variables that were related significantly to the occurrence of HAT are also interrelated. A multivariate analysis failed to identify any one of them as an independent risk factor for thrombosis unless not considering the heparin treatment.

The level of the anastomosis did not correlate with the incidence of thrombosis. However, this finding may be related to the influence of other factors. For example, the level of the anastomosis is often determined by vessel size in order to have the best match between donor and recipient arteries. Also, sometimes the level of reconstruction is determined by whether an anastomosis has required revision; both the size of the vessel and the number of times that the anastomosis has required revision are known risk factors, therefore the influence of the level of the anastomosis on the occurrence of thrombosis cannot definitively be ruled out. The splenic artery ligation performed in two patients of this series was not burdened with complications—however, because of the small number of cases the prophylactic ligation of splenic artery requires further evaluation.

The perioperative and intraoperative coagulation profiles were not significantly different between the two groups studied (Table 3, part I). Blood loss and the quantity of transfusions have previously been correlated with survival in children after OLTx (*20*). In our study the quality of transfusion, instead of quantity, has resulted in a significant difference. The incidence of HAT was significantly higher in children who received intraoperative transfusion of FFP compared with children who did not receive any FFP at all. There is no documentation that FFP has a beneficial effect when used as a part of transfusion management of patients with massive hemorrhage; in acute blood loss, alternative therapies are equally satisfactory and considerably safer (*21*). The only indication for FFP administration in cases of massive blood transfusion is when factors V and VIII are less than 25% of normal, as documented by laboratory measurement (*22*). The intraoperative use of FFP in pediatric liver recipients should be curtailed and used only when gross deficiency of coagulation factors has been demonstrated by an assay.

The use of postoperative anticoagulation correlated significantly ($P<.01$) with patency of the hepatic artery after liver transplantation. This event is not surprising, since antithrombotic therapy is an essential tool in intensive care and preventive medicine (*23, 25*). Dextran-40 and heparin appeared to be particularly effective in preventing hepatic artery thrombosis (Table 3, part II). The risk (odds ratio) of developing HAT in patients who did not receive anticoagulant therapy was almost 8 and 5 times greater than in patients who received heparin and dextran, respectively (Fig. 2). After a multivariate analysis, anticoagulation therapy surfaced as the only independent variable influencing hepatic artery thrombosis.

However, caution must be exercised in the interpretation of these results. The anticoagulation therapy, in fact, was not given in a controlled fashion because of the preliminary nature of this study. Although our results could be biased by including patients thought to be at high risk of thrombosis in the study, the postoperative anticoagulative therapy appears to be a statistically independent factor in preventing HAT. There are no other reports in the literature regarding the use of anticoagulants in pediatric liver recipients to prevent HAT. If corroborated by other controlled prospective studies, routine prophylactic administration of anticoagulant could be advocated, at least in the high-risk patients.

Dextran has to be started intraoperatively to have the best effect (*23*). At the dosage used, allergic reactions and renal failure were not encountered. Similarly heparin was tolerated well. In a few patients with bleeding, temporary reduction of the dosage was effective in controlling the bleeding without further treatment.

Because of the small number of cases, the full importance of either aspirin or persantine cannot be completely assessed in this study, even if their role in maintaining an appropriate long-term coagulative state seems to be important.

It should be remembered that any severe coagulopathy due to early posttransplant liver failure has been excluded from the present study. These patients, in fact, might be expected to have a higher incidence of thrombosis because of poor perfusion of the liver and subsequent edema that compounds the problem

with poor hepatic artery flow.

Other factors associated with HAT might include variables specific to the new liver itself, such as ischemia/reperfusion damage with endothelial swelling and different grades of rejection. Indirect proof of the importance of the former mechanism is evident from our current experience with the use of the new University of Wisconsin lactobionate liver preservation solution (*26*).

The incidence of HAT after initiation of use of the lactobionate solution at the University of Pittsburgh (both adult and pediatric) appears considerably decreased compared with the period when Euro-Collins solution was being used (*27*). Better endothelial and parenchymal cell preservation undoubtedly has a strong influence on the maintenance of the microvascular circulation, (*26, 28*) and therefore on the whole arterial and venous patency distal to the anastomosis.

In summary, this is the first detailed and analytical retrospective report on hepatic artery thrombosis after liver transplantation in pediatric patients. The study has described a large number of variables that may influence the development of this complication—but, most important, has identified a group of factors that correlate statistically with the thrombotic event. The importance of an anticoagulation protocol following liver transplantation in high-risk patients is readily apparent. The results of this study should serve as a guideline for future prospective studies, and for the development of medicosurgical therapeutic protocols to overcome this dramatic complication.

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Received 21 June 1988.
Accepted 28 November 1988.